```
     FILE 'HCAPLUS' ENTERED AT 14:54:30 ON 28 APR 2009
L1        31321 S HERPES OR HSV OR HSV1 OR HSV2
L2         1224 S ((ACYCLOVIR OR GANCYCLOVIR OR NUCLEOSIDE)(W)(PHOSPHATE OR PHO
L3          102 S L1 AND L2
L4           72 S L3 AND (PY<2003 OR AY<2003 OR PRY<2003)

     FILE 'STNGUIDE' ENTERED AT 14:54:36 ON 28 APR 2009

     FILE 'HCAPLUS' ENTERED AT 14:55:16 ON 28 APR 2009
L5        10514 S THYMIDINE KINASE
L6           11 S L4 AND L5
```

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=> file hcaplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.88       0.88

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FILE COVERS 1907 - 28 Apr 2009  VOL 150 ISS 18
FILE LAST UPDATED: 27 Apr 2009  (20090427/ED)

HCAplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2008.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s herpes or HSV or HSV1 or HSV2

         29038 HERPES
         13859 HSV
          2213 HSV1
           477 HSV2
L1       31321 HERPES OR HSV OR HSV1 OR HSV2

=> s ((acyclovir or gancyclovir or nucleoside)(w)(phosphate or phosphonate)) or
PMEA or (phosphonomethoxyethyl adenine) or phosphonomethoxyethyladenine

          4492 ACYCLOVIR
           383 GANCYCLOVIR
         52490 NUCLEOSIDE
        624026 PHOSPHATE
         27442 PHOSPHONATE
           778 (ACYCLOVIR OR GANCYCLOVIR OR NUCLEOSIDE)(W)(PHOSPHATE OR PHOSPHO
               NATE)
           488 PMEA
            90 PHOSPHONOMETHOXYETHYL
         62677 ADENINE
            51 PHOSPHONOMETHOXYETHYL ADENINE
                 (PHOSPHONOMETHOXYETHYL(W)ADENINE)
            25 PHOSPHONOMETHOXYETHYLADENINE
L2         1224 ((ACYCLOVIR OR GANCYCLOVIR OR NUCLEOSIDE)(W)(PHOSPHATE OR PHOSPH
               ONATE)) OR PMEA OR (PHOSPHONOMETHOXYETHYL ADENINE) OR PHOSPHONOM
               ETHOXYETHYLADENINE
```

```
=> s l1 and l2

L3         102 L1 AND L2

=> s l3 and (PY<2003 or AY<2003 or PRY<2003)

      22984005 PY<2003
       4506202 AY<2003
       3975570 PRY<2003
L4           72 L3 AND (PY<2003 OR AY<2003 OR PRY<2003)

=> file stnguide

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       2.85       3.73

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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Apr 24, 2009 (20090424/UP).

=> file hcaplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.07       3.80

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FILE COVERS 1907 - 28 Apr 2009  VOL 150 ISS 18
FILE LAST UPDATED: 27 Apr 2009  (20090427/ED)

HCAplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2008.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s thymidine kinase
```

```
         57011 THYMIDINE
        348113 KINASE
L5       10514 THYMIDINE KINASE
                (THYMIDINE(W)KINASE)

=> s l4 and l5

L6          11 L4 AND L5

=> file stnguide

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       2.85       6.65

FILE 'STNGUIDE' ENTERED AT 14:55:18 ON 28 APR 2009
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Apr 24, 2009 (20090424/UP).

=> d l6 1-11 ti abs bib
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y



L6   ANSWER 1 OF 11  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   Resistance of herpesviruses to antiviral drugs: Clinical impacts and
     molecular mechanisms
AB   A review.  Nucleoside analogs such as acyclovir and ganciclovir have been
     the mainstay of therapy for alphaherpesviruses [herpes simplex
     virus (HSV) and varicella-zoster virus (VZV)] and
     cytomegalovirus (CMV) infections, resp.  Drug-resistant herpesviruses are
     found relatively frequently in the clinic, almost exclusively among
     severely immunocompromised patients receiving prolonged antiviral therapy.
     For instance, close to 10% of patients with AIDS receiving i.v.
     ganciclovir for 3 mo excrete a drug-resistant CMV isolate in their blood
     or urine and this percentage increases with cumulative drug exposure.
     Many studies have reported that at least some of the drug-resistant
     herpesviruses retain their pathogenicity and can be associated with
     progressive or relapsing disease.  Viral mutations conferring resistance
     to nucleoside analogs have been found in either the drug
     activating/phosphorylating genes (HSV or VZV thymidine
     kinase, CMV UL97 kinase) and/or in conserved regions of the viral
     DNA polymerase.  Currently available second line agents for the treatment
     of herpesvirus infections-the pyrophosphate analog foscarnet and the
     acyclic nucleoside phosphonate derivative cidofovir-also
     inhibit the viral DNA polymerase but are not dependent on prior
     viral-specific activation.  Hence, viral DNA polymerase mutations may lead
     to a variety of drug resistance patterns which are not totally predictable
     at the moment due to insufficient information on specific drug binding
     sites on the polymerase.  Although some CMV and HSV DNA
     polymerase mutants have been found to replicate less efficiently in cell
     cultures, further research is needed to correlate viral fitness and clin.
     outcome.
AN   2002:856088  HCAPLUS <<LOGINID::20090428>>
DN   138:2047
TI   Resistance of herpesviruses to antiviral drugs: Clinical impacts and
     molecular mechanisms
```

AU Gilbert, Christian; Bestman-Smith, Julie; Boivin, Guy
CS Research Center in Infectious Diseases, Centre Hospitalier Universitaire de Quebec and Laval University, Quebec City, QC, Can.
SO Drug Resistance Updates (2002), 5(2), 88-114
CODEN: DRUPFW; ISSN: 1368-7646
PB Elsevier Science Ltd.
DT Journal; General Review
LA English
RE.CNT 197 THERE ARE 197 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Design, Synthesis, and Biological Evaluation of Novel Nucleoside and Nucleotide Analogues as Agents against DNA Viruses and/or Retroviruses
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A novel strategy was developed for the synthesis of N7-purine acyclic nucleosides. The key step involved the reaction between [2-(p-methoxyphenyloxy)ethoxy]methyl chloride and N9-tritylated nucleobases followed by concomitant self-detritylation. The N7-guanine acyclic nucleoside exhibited antiviral activity, but was phosphorylated by both HSV and Vero cell thymidine kinases; thus, it showed more potent cellular toxicity than acyclovir. The N7-adenine acyclic nucleoside was found to be an excellent antiviral agent as well as a good inhibitor of calf mucosal adenosine deaminase. This inhibitory property allows for a greater expression of antiviral activity of antiviral agents, such as N9-adenine acyclic nucleoside and ara-A. The N7-adenine acyclic nucleoside was phosphorylated neither by herpes simplex virus (HSV) thymidine kinase nor by Vero cell thymidine kinase, yet it enhanced the rate constant for the monophosphorylation of acyclovir by HSV thymidine kinase. Consequently, the combination of acyclovir and N7-adenine acyclic nucleoside exhibited greater antiviral activity than acyclovir alone. 7-[2-(Phosphonomethoxy)ethyl]adenine was also synthesized. The key step involved the reaction of 9-(2-cyanoethyl)adenine with Me iodoacetate in the presence of lithium 2,2,6,6-tetramethylpiperidine in THF. Unlike 9-[2-(phosphonomethoxy)ethyl]adenine (PMEA), the N7-isomer was not phosphorylated effectively by 5-phosphoribosyl 1-pyrophosphate synthetase (PRPP synthetase); thus, it did not exhibit pronounced antiviral activity. An adenine dinucleotide 5'-monophosphate I and its butenolide ester were also synthesized. Compound I showed substrate activity toward PRPP synthetase and exhibited notable activity against DNA viruses. The antiviral activity of the butenolide ester derivative was found to be higher than that of the parent mol. Compound I is susceptible to degradation by snake venom and spleen phosphodiesterases. However, its resp. butenolide ester derivative was completely resistant to snake venom and spleen enzymes. Guanine and adenine butenolide ester derivs. II (R1 = NH2, R2 = H; R1 = OH, R2 = NH2) were also synthesized and exhibited notable anti-DNA virus and anti-retrovirus activity in vitro. Final compds. were evaluated for their inhibitory effect on HSV-1-induced mortality in NMRI mice. The N7-adenine acyclic nucleoside [LD50 (i.p.) 950 mg/kg], the butenolide ester of I [LD50 (i.p.) 675 mg/kg], and II (R1 = NH2, R2 = H)[LD50 (i.p.) 710 mg/kg] were found to be potent anti-HSV-1 agents in vivo. In addition, II (R1 = NH2, R2 = H) efficiently decreased tumor formation induced by Moloney murine sarcoma virus (MSV) in NMRI mice while significantly increasing the survival time of MSV-infected mice.

AN 2001:677297 HCAPLUS <<LOGINID::20090428>>
DN 135:371947
TI Design, Synthesis, and Biological Evaluation of Novel Nucleoside and Nucleotide Analogues as Agents against DNA Viruses and/or Retroviruses
AU Hakimelahi, Gholam Hossein; Ly, Tai Wei; Moosavi-Movahedi, Ali A.; Jain, Moti L.; Zakerinia, Maryam; Davari, Hady; Mei, Hui-Ching; Sambaiah, Thota; Moshfegh, Ali A.; Hakimelahi, Shahram
CS Institute of Chemistry, Academia Sinica, Taipei, 115, Taiwan
SO Journal of Medicinal Chemistry (2001), 44(22), 3710-3720
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 135:371947
RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Antiviral drugs against herpes infections
AB A review with 34 refs. Several new and promising antiviral drugs have been approved which allow better options to control infections caused by herpes virus. Vidarabine has been the earliest available drug against herpes simplex (HSV) and varicella zoster (VZV), but is an agent that is rarely used at present. Acyclovir has replaced vidarabine in treating herpes infections in immunocompetent and immuno compromised patients. The low oral bioavailability of acyclovir, as well as emergence of drug resistant strains have stimulated efforts towards development of newer compds. for treatment of herpes infection. These include penciclovir and its oral prodrug famciclovir and the oral prodrug form of acyclovir, valacyclovir. These drugs are dependent on virus encoded thymidine kinase (TK) for their intracellular activation (phosphorylation) and, upon conversion to their triphosphate form which act as inhibitors/alternative substrate of viral DNA polymerase. Therefore resistance of these drugs may occur for virus mutants that are TK-deficient. Newer drugs as Sorivudine which is a nucleoside analog has been pursued in treating herpes infections. Foscarnet, which does not require any previous metabolism to interact with viral DNA polymerase is useful in clin. settings when TK deficient mutant strains emerge. Cidofovir, an acyclic nucleoside phosphonate is yet another available drug to which TK deficients strains are sensitive. This review describes these currently available antiviral drugs against herpes virus, some approved and others under clin. evaluation for approval.
AN 2001:48798 HCAPLUS <<LOGINID::20090428>>
DN 135:131486
TI Antiviral drugs against herpes infections
AU Vajpayee, Madhu; Malhotra, Neena
CS Department of Microbiology, All India Institute of Medical Sciences, New Delhi, 110 029, India
SO Indian Journal of Pharmacology (2000), 32(6), 330-338
CODEN: INJPD2; ISSN: 0253-7613
PB Indian Pharmacological Society
DT Journal; General Review
LA English
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Hydroxyurea potentiates the antiherpesvirus activities of purine and pyrimidine nucleoside and nucleoside phosphonate

analogs
AB Hydroxyurea has been shown to potentiate the anti-human immunodeficiency virus activities of 2',3'-dideoxynucleoside analogs such as didanosine. We have now evaluated in vitro the effect of hydroxyurea on the antiherpesvirus activities of several nucleoside analogs (acyclovir [ACV], ganciclovir [GCV], penciclovir [PCV], lobucavir [LBV], (R)-9-[4-hydroxy-2-(hydroxymethyl)butyl]guanine [H2G], and brivudin and nucleoside phosphonate analogs (cidofovir [CDV] and adefovir [ADV]). When evaluated in cytopathic effect (CPE) reduction assays, hydroxyurea by itself had little effect on CPE progression and potentiated in a subsynergistic (herpes simplex virus type 1 [HSV -1]) to synergistic (HSV-2) fashion the antiviral activities of ACV, GCV, PCV, LBV, H2G, ADV, and CDV. Hydroxyurea also caused marked increases in the activities of ACV, GCV, PCV, LBV, and H2G (compds. that depend for their activation on a virus-encoded thymidine kinase [TK]) against TK-deficient (TK-) HSV-1. In fact, in combination with hydroxyurea the 50% effective concns. of these compds. for inhibition of TK- HSV-1-induced CPE decreased from values of 20 to ≥100 μg/mL (in the absence of hydroxyurea) to values of 1 to 5 μg/mL (in the presence of hydroxyurea at 25 to 100 μg/mL). When evaluated in a single-cycle virus yield reduction assay, hydroxyurea at a concentration of 100 μg/mL inhibited progeny virus production by 60 to 90% but had little effect on virus yield at a concentration of 25 μg/mL. Under these assay conditions hydroxyurea still elicited a marked potentiating effect on the antiherpesvirus activities of GCV and CDV, but this effect was less pronounced than that in the CPE reduction assay. It is conceivable that the potentiating effect of hydroxyurea stems from a depletion of the intracellular deoxynucleoside triphosphate pools, thus favoring the triphosphates of the nucleoside analogs (or the diphosphates of the nucleoside phosphonate analogs) in their competition with the natural nucleotides at the viral DNA polymerase level. The possible clin. implications of these findings are discussed.
AN 1999:784932 HCAPLUS <<LOGINID::20090428>>
DN 132:117100
TI Hydroxyurea potentiates the antiherpesvirus activities of purine and pyrimidine nucleoside and nucleoside phosphonate analogs
AU Neyts, J.; De Clercq, E.
CS Rega Institute for Medical Research, Louvain, B-3000, Belg.
SO Antimicrobial Agents and Chemotherapy (1999), 43(12), 2885-2892 CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Nucleoside analog phosphates for topical use in the treatment of herpes virus infections
AB Compns. for topical use in herpes virus infections comprise anti-herpes nucleoside analog phosphate esters, e.g. acyclovir monophosphate, acyclovir diphosphate, and acyclovir triphosphate which show increased activity against native strains of herpes virus as well as against resistant strains, particularly thymidine kinase neg. strains of virus. Also disclosed are methods for treatment of herpes infections with nucleoside phosphates. Anti-herpes nucleoside analogs phosphate esters include the phosphoramidates and phosphothiorates, as well as polyphosphates comprising C and S bridging atoms.

AN 1999:175589 HCAPLUS <<LOGINID::20090428>>
DN 130:218263
TI Nucleoside analog phosphates for topical use in the treatment of herpes virus infections
IN Hostetler, Karl Y.
PA USA
SO U.S., 19 pp., Cont.-in-part of U.S. 5,580,571.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5879700	A	19990309	US 1995-480456	19950607 <--
	US 5580571	A	19961203	US 1993-60258	19930512 <--
	CA 2222154	A1	19961219	CA 1996-2222154	19960606 <--
	WO 9640088	A1	19961219	WO 1996-US10085	19960606 <--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
	AU 9663842	A	19961230	AU 1996-63842	19960606 <--
	EP 831794	A1	19980401	EP 1996-923289	19960606 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	CN 1192138	A	19980902	CN 1996-195922	19960606 <--
	JP 11507642	T	19990706	JP 1997-502194	19960606 <--
	CN 1221609	A	19990707	CN 1998-123863	19981030 <--
PRAI	US 1991-777683	B2	19911015	<--	
	US 1993-60258	A2	19930512	<--	
	US 1995-480456	A	19950607	<--	
	WO 1996-US10085	W	19960606	<--	

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Acyclovir derivatives for topical use
AB The invention involves compns. for topical use in herpes virus infections comprising anti-herpes nucleoside analog phosphate esters, such as acyclovir monophosphate, acyclovir diphosphate, and acyclovir triphosphate, which show increased activity against native strains of herpes virus as well as against resistant strains, particularly thymidine kinase neg. strains of virus. Anti-herpes nucleoside analogs phosphate esters include the phosphoramidates and phosphothiorates, as well as polyphosphates comprising C and S bridging atoms.
AN 1997:121416 HCAPLUS <<LOGINID::20090428>>
DN 126:135594
OREF 126:26139a,26142a
TI Acyclovir derivatives for topical use
IN Hostetler, Karl Y.
PA Hostetler, Karl Y., USA
SO PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 9640088 A1 19961219 WO 1996-US10085 19960606 <--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN
US 5879700 A 19990309 US 1995-480456 19950607 <--
AU 9663842 A 19961230 AU 1996-63842 19960606 <--
EP 831794 A1 19980401 EP 1996-923289 19960606 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
JP 11507642 T 19990706 JP 1997-502194 19960606 <--
PRAI US 1995-480456 A 19950607 <--
US 1991-777683 B2 19911015 <--
US 1993-60258 A2 19930512 <--
WO 1996-US10085 W 19960606 <--
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Nucleoside analogs for topical use in herpesvirus infections
AB Compns. for topical use in herpesvirus infections comprise anti-herpes nucleoside analog phosphate esters, such as acyclovir monophosphate and acyclovir diphosphate, which show increased activity against native strains of herpesvirus as well as against resistant strains, particularly thymidine kinase-neg. strains of the virus. Thus, acyclovir monophosphate was more effective than acyclovir in treatment of lesions in mice infected with an acyclovir-resistant strain of herpes simplex virus type 1. Acyclovir monophosphate was prepared by reaction of acyclovir with POCl3 in P(O)(OMe)3 followed by neutralization with aqueous NaOH.
AN 1996:754377 HCAPLUS <<LOGINID::20090428>>
DN 126:70124
OREF 126:13441a,13444a
TI Nucleoside analogs for topical use in herpesvirus infections
IN Hostetler, Karl Y.
PA Hostetler, Karl Y., USA
SO U.S., 14 pp., Cont.-in-part of U.S. Ser. No. 777,683, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5580571	A	19961203	US 1993-60258	19930512 <--
	US 5654286	A	19970805	US 1995-485025	19950607 <--
	US 5879700	A	19990309	US 1995-480456	19950607 <--
	US 5756116	A	19980526	US 1996-758501	19961202 <--
	US 6015573	A	20000118	US 1997-991740	19971216 <--
PRAI	US 1991-777683	B2	19911015 <--		
	US 1993-60258	A2	19930512 <--		
	US 1996-758501	A1	19961202 <--		

OS CASREACT 126:70124
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Phenotypic resistance of herpes simplex virus type 1 strains selected in vitro with antiviral compounds and combinations thereof
AB Several drug resistant herpes simplex virus type 1 (HSV

-1) strains were obtained under the selective pressure of various antiherpetic drugs used alone or in combination. Their susceptibility to a wide range of antiviral compds. was determined Strains selected under the pressure of brivudine (BVDU) or 1-β-D-arabino-furanosyl-(E)-5-(2-bromovinyl)uracil (BVaraU) alone were composed of two virus populations: (1) virus resistant to BVDU and BVaraU bot not to acyclovir (ACV) or ganciclovir (GCV), which is suggestive of an alteration in the thymidylate kinase activity associated with viral thymidine kinase (TK) (responsible for the phosphorylation of BVDU-monophosphate to BVDU-diphosphate); and (2) virus resistant to TK-dependent drugs (i.e. ACV, GCV, BVDU and BVaraU) as well as double-mutant strains with decreased sensitivity to both TK-dependent compds. and the pyrophosphate analogs foscarnet (PFA) and phosphonoacetic acid (PAA) (suggestive of mutations at the level of the DNA polymerase) were recovered under the selective pressure of ACV alone or in combination with BVDU or BVaraU. Combinations of BVDU or BVaraU with PFA or PAA led to strains resistant only to BVDU and BVaraU or double-mutant strains resistant to BVDU, BVaraU and the pyrophosphate analogs, but not to strains resistant to other TK-dependent drugs. Interestingly, strains resistant to ACV, BVDU, GCV and/or the pyrophosphate analogs PFA and PAA remained sensitive to the (S)-3-hydroxy-2-phosphonyl-methoxypropyl (HPMP) derivs. of cytosine (HPMPC) and adenine (HPMPA).

AN 1996:594451 HCAPLUS <<LOGINID::20090428>>
DN 125:292318
OREF 125:54375a,54378a
TI Phenotypic resistance of herpes simplex virus type 1 strains selected in vitro with antiviral compounds and combinations thereof
AU Morfin, F.; Snoeck, R.; Andrei, G.; De Clercq, E.
CS Rega Inst. Med. Res., Katholieke Universiteit Leuven, Louvain, B-3000, Belg.
SO Antiviral Chemistry & Chemotherapy (1996), 7(5), 270-275
CODEN: ACCHEH; ISSN: 0956-3202
PB Blackwell
DT Journal
LA English

L6 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Acyclic nucleosides as antiviral compounds
AB A review with 94 refs. Acyclovir is an effective drug for the treatment of HSV and VZV infections, which after phosphorylation to the triphosphate, inhibits viral DNA polymerase. Acyclovir has low oral bioavailability, therefore prodrugs have been developed, and the L-valyl ester, valaciclovir, recently has been licensed for the treatment of shingles. Ganciclovir is used against CMV, and famciclovir, a lipophilic prodrug of penciclovir, is marketed for shingles. The acyclic nucleoside phosphonates are active against thymidine kinase -resistant viral strains. Promising analogs are PMEA (in clin. trial for the treatment of AIDS) and (S)-HPMPC (good in vivo activity against HSV, VZV, CMV, and EBV). Oligonucleotides incorporating acyclic nucleosides at the 3'- and 5'-ends, or constituted of amino acyclic nucleosides, are resistant to cleavage by nucleases and may be useful in antisense and/or antigene therapy. HEPT is active against HIV-1:. It binds in a hydrophobic pocket on reverse transcriptase, rather than in the polymerase active site. Some acyclic nucleosides are potent inhibitors of purine and pyrimidine nucleoside phosphorylase. These compds. may have a therapeutic niche in combination therapy with antiviral and anticancer nucleosides, and in the treatment of diseases involving the T-cell.

AN 1996:420923 HCAPLUS <<LOGINID::20090428>>
DN 125:75098
OREF 125:14003a,14006a

TI Acyclic nucleosides as antiviral compounds
AU Freeman, Sally; Gardiner, John M.
CS Department Pharmacy, University Manchester, Manchester, M139PL, UK
SO Molecular Biotechnology (1996), 5(2), 125-137
CODEN: MLBOEO; ISSN: 1073-6085
PB Humana
DT Journal; General Review
LA English

L6 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Inhibitors of bovine herpes mammillitis virus infections in cultured cells and in vaginally infected guinea pigs
AB Bovine herpes mammillitis virus or bovine herpesvirus type 2 (BHV-2) causes ulcerative lesions on the teats and udders of infected cows. The authors investigated several nucleoside and nucleotide analogs as potential BHV-2 inhibitors. These included acyclovir, ganciclovir, 5-iodo-2'-deoxyuridine (IUdR), 1-(2'-deoxy-2'-fluoro-β-D-arabinofuranosyl) derivs. of 5-iodocytosine (FIAC), 5-iodouracil (FIAU), and 5-methyluracil (FMAU), and various 3-hydroxyphosphonylmethoxypropyl (HPMP) and 2-phosphonylmethoxyethyl (PME) derivs. of adenine (A), guanine (G), 2,6-diaminopurine (DAP), and/or cytosine (C). Of these, FIAU and FMAU were the most potent in cell culture, inhibiting 50% of BHV-2 plaques at <0.05 μM. HPMPA and HPMPG were active at 0.3 μM; FIAC, IUdR, and HPMPC at 1.3-2.3 μM; PMEDAP and ganciclovir at 20-25 μM; acyclovir and PMEA at >100 μM. The two most potent agents, FIAU and FMAU, inhibited uninfected embryonic bovine tracheal cell growth by 50% at >100 μM and 53 μM, resp., resulting in selectivity indexes (ratio of the 50% inhibitory concentration for cell growth to the 50% inhibitory concentration for plaque formation) of >2200 and 1100. Greater degrees of antiviral activity and selectivity were obtained in infected guinea pig embryo cells treated with FIAU, FMAU, and HPMPC. Infected cell exts. containing BHV-2-induced thymidine kinase activity phosphorylated FIAU, FMAU, and IUdR at nearly the same rate as thymidine, whereas FIAC, acyclovir, and ganciclovir were phosphorylated at ≤5% the rate of thymidine. Phosphorylation by this enzyme is required to generate the antivirally active nucleoside triphosphate in infected cells. In guinea pigs infected intravaginally with BHV-2, FMAU treatments of 1, 3.2, and 10 mg kg-1 per day for 5 days starting 1 day after virus challenge reduced vaginal lesion scores and virus titers in a dose-dependent manner. FIAU (10 μM) was as effective as 1 μM FMAU by the same regimen. A single treatment with 10 μM HPMPC was as active as daily treatments with 3.2 mg FMAU kg-1. These results indicate the potential of using antiviral agents to treat bovine herpes mammillitis virus infections in cattle, and the application of guinea pigs to study BHV-2 disease.
AN 1994:671329 HCAPLUS <<LOGINID::20090428>>
DN 121:271329
OREF 121:49243a,49246a
TI Inhibitors of bovine herpes mammillitis virus infections in cultured cells and in vaginally infected guinea pigs
AU Smee, D. F.; Leonhardt, J. A.; Sugiyama, S. T.; Holy, A.
CS Inst. Antiviral Res., Utah State Univ., Logan, UT, 84322-5600, USA
SO Antiviral Chemistry & Chemotherapy (1994), 5(4), 201-8
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DT Journal
LA English

L6 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Properties of a 9-(2-phosphonylmethoxyethyl)adenine (PMEA)-resistant herpes simplex virus type 1 virus mutant
AB After repeated passages of herpes simplex type 1 (HSV

-1) KOS virus in the presence of 9-(2-phosphonylmethoxyethyl)adenine (PMEA), a mutant denoted PMEAr HSV-1 was isolated which grew well in the presence of 50-100 μg/mL of the drug. PMEAr HSV-1 was still sensitive to the related phosphonate analog (S)-9-(3-hydroxy-2-phosphonylmethoxypropyl)adenine (HPMPA). In fact, it was more susceptible to the action of HPMPA than the original virus. PMEAr HSV-1 also retained sensitivity to 5-bromo-2'-deoxyuridine and other, viral thymidine kinase-dependent substances such as (E)-5-(2-bromovinyl)-2'-deoxyuridine. However, PMEAr HSV -1 was much less sensitive to acyclovir, 1-(β-D-arabinofuranosyl)cytosine and 1-(β-D-arabinofuranosyl)thymine than the parental KOS virus.

AN 1990:627872 HCAPLUS <<LOGINID::20090428>>
DN 113:227872
OREF 113:38365a,38368a
TI Properties of a 9-(2-phosphonylmethoxyethyl)adenine (PMEA)-resistant herpes simplex virus type 1 virus mutant
AU Vonda, Vladimir; Anisimova, Emma; Cerny, Jaroslav; Holy, Antonin; Rosenberg, Ivan; Votruba, Ivan
CS Dep. Exp. Virol., Inst. Sera Vaccines, Prague, 101 03, Czech.
SO Antiviral Research (1990), 14(2), 117-21
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LA English